

WHAT IS CLAIMED IS:

1. A portable DNA sequence comprising a series of nucleotides capable of directing intracellular production of metalloproteinase inhibitors.
2. The portable DNA sequence of claim 1 wherein said sequence is capable of directing intracellular production of collagenase inhibitors.
3. The portable DNA sequence of claim 1 wherein said nucleotide sequence is:

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      10      20      30      40      50      60
GTTGTTGCTG TGGCTGATAG CCCCAGCAGG GCCTGCACCT GTGTCCCACC CCACCCACAG

      70      80      90     100     110     120
ACGGCCTTCT GCAATTCCGA CCTCGTCATC AGGGCCAAGT TCGTGGGGAC ACCAGAAGTC

     130     140     150     160     170     180
AACCAGACCA CCTTATACCA GCGTTATGAG ATCAAGATGA CCAAGATGTA TAAAGGGTTC

     190     200     210     220     230     240
CAAGCCTTAG GGGATGCCGC TGACATCCGG TTCGTCTACA CCCCCGCCAT GGAGAGTGTC

     250     260     270     280     290     300
TGCGGATACT TCCACAGGTC CCACAACCGC AGCGAGGAGT TTCTCATTGC TGGAAACTG

     310     320     330     340     350     360
CAGGATGGAC TCTTGACAT CACTACCTGC AGTTTCGTGG CTCCCTGGAA CAGCCTGAGC

     370     380     390     400     410     420
TTAGCTCAGC GCCGGGGCTT CACCAAGACC TACACTGTTG GCTGTGAGGA ATGCACAGTG

     430     440     450     460     470     480
TTTCCCTGTT TATCCATCCC CTGCAAACTG CAGAGTGGCA CTCATTGCTT GTGGACGGAC

     490     500     510     520     530     540
CAGCTCCTCC AAGGCTCTGA AAAGGGCTTC CAGTCCCGTC ACCTTGCCCTG CCTGCCTCGG

     550     560     570     580     590     600
GAGCCAGGGC TGTGCACCTG GCAGTCCCTG CGGTCCCAGA TAGCCTGAAT CCTGCCCCGA

     610     620     630     640     650     660
GTGGAAGCTG AAGCCTGCAC AGTGTCCACC CTGTTCCAC TCCCATCTTT CTTCCGGACA

     670     680     690     700
ATGAAATAAA GAGTTACCAC CCAGCAAAAA AAAAAAGGAA TTC
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4. The portable DNA sequence of claim 2 wherein said sequence is capable of directing intracellular production of a collagenase inhibitor biologically equivalent to that isolable from human skin fibroblasts.

5. A recombinant-DNA cloning vector comprising a nucleotide sequence capable of directing intracellular production of metalloproteinase inhibitors.

6. The vector of claim 5 wherein said vector comprises a nucleotide sequence containing at least the following nucleotides:

10 20 30 40 50 60
GTTGTTGCTG TGGCTGATAG CCCAGCAGG GCCTGCACCT GTGTCCCACC CCACCCACAG
70 80 90 100 110 120
ACGGCCTTCT GCAATTCCGA CCTCGTCATC AGGGCCAAGT TCGTGGGGAC ACCAGAAGTC
130 140 150 160 170 180
AACCAGACCA CCTTATACCA GCGTTATGAG ATCAAGATGA CCAAGATGTA TAAAGGGTTC
190 200 210 220 230 240
CAAGCCTTAG GGGATGCCGC TGACATCCGG TTCGTCTACA CCCCCGCCAT GGAGAGTGTC
250 260 270 280 290 300
TGCGGATACT TCCACAGGTC CCACAACCGC AGCGAGGAGT TTCTCATTGC TGGAAACTG
310 320 330 340 350 360
CAGGATGGAC TCTTGACAT CACTACCTGC AGTTTCGTGG CTCCCTGGAA CAGCCTGAGC
370 380 390 400 410 420
TTAGCTCAGC GCCGGGGCTT CACCAAGACC TACACTGTTG GCTGTGAGGA ATGCACAGTG
430 440 450 460 470 480
TTTCCCTGTT TATCCATCCC CTGCAAACTG CAGAGTGGCA CTCATTGCTT GTGGACGGAC
490 500 510 520 530 540
CAGCTCCTCC AAGGCTCTGA AAAGGGCTTC CAGTCCCGTC ACCTTGCCCTG CCTGCCTCGG
550 560 570 580 590 600
GAGCCAGGGC TGTGCACCTG GCAGTCCCTG CGGTCCCAGA TAGCCTGAAT CCTGCCCCGA
610 620 630 640 650 660
GTGGAAGCTG AAGCCTGCAC AGTGTCCACC CTGTTCCAC TCCCATCTTT CTTCCGGACA
670 680 690 700
ATGAAATAAA GAGTTACCAC CCAGCAAAAA AAAAAAGGAA TTC

7. The vector pUC9-F5/237P10.

8. A recombinant-DNA method for microbial production of a

metalloproteinase inhibitor comprising:

- (a) preparation of a portable DNA sequence capable of directing a host microorganism to produce a protein having metalloproteinase inhibitor activity;
- (b) cloning the portable DNA sequence into a vector capable of being transferred into and replicating in a host microorganism, such vector containing operational elements for the portable DNA sequence;
- (c) transferring the vector containing the portable DNA sequence and operational elements into a host microorganism capable of expressing the metalloproteinase inhibitor protein;
- (d) culturing the host microorganism under conditions appropriate for amplification of the vector and expression of the inhibitor; and
- (e) in either order:
 - (i) harvesting the inhibitor; and
 - (ii) causing the inhibitor to assume an active, tertiary structure whereby it possesses metalloproteinase inhibitor activity.

9. The method of claim 8 wherein said metalloproteinase inhibitor is collagenase inhibitor.

10. The method of claim 8 wherein said portable DNA sequence is:

10 20 30 40 50 60
GTTGTTGCTG TGGCTGATAG CCCCAGCAGG GCCTGCACCT GTGTCCCACC CCACCCACAG
70 80 90 100 110 120
ACGGCCTTCT GCAATTCCGA CCTCGTCATC AGGGCCAAGT TCGTG GGGGAC ACCAGAAGTC
130 140 150 160 170 180
AACCAGACCA CTTTATACCA GCGTTATGAG ATCAAGATGA CCAAGATGTA TAAAGGGTTC
190 200 210 220 230 240
CAAGCCTTAG GGGATGCCGC TGACATCCGG TTCGTCTACA CCCCCGCCAT GGAGAGTGTC
250 260 270 280 290 300
TGCGGATACT TCCACAGGTC CCACAACCGC AGCGAGGAGT TTCTCATTGC TGGAAAAGT
310 320 330 340 350 360
CAGGATGGAC TCTTGACAT CACTACCTGC AGTTTCGTGG CTCCCTGGAA CAGCCTGAGC
370 380 390 400 410 420
TTAGCTCAGC GCCGGGGCTT CACCAAGACC TACACTGTTG GCTGTGAGGA ATGCACAGTG
430 440 450 460 470 480
TTTCCCTGTT TATCCATCCC CTGCAAAGT CAGAGTGGCA CTCATTGCTT GTGGACGGAC
490 500 510 520 530 540
CAGCTCCTCC AAGGCTCTGA AAAGGGCTTC CAGTCCCGTC ACCTTGCCCTG CCTGCCTCGG
550 560 570 580 590 600
GAGCCAGGGC TGTGCACCTG GCAGTCCCTG CGGTCCCAGA TAGCCTGAAT CCTGCCCCGA
610 620 630 640 650 660
GTGGAAGCTG AAGCCTGCAC AGTGTCCACC CTGTTCCCAC TCCCATCTTT CTTCCGGACA
670 680 690 700
ATGAAATAAA GAGTTACCAC CCAGCAAAAA AAAAAAGGAA TTC

11. The method of claim 8 wherein said vector containing said portable DNA sequence is pUC9-F5/237P10.

12. The method of claim 8 wherein said host microorganism is a bacterium.

13. The method of claim 12 wherein said bacterium is a member of the genus *Bacillus*.

14. The method of claim 13 wherein said bacterium is *Bacillus subtilis*.

15. The method of claim 12 wherein said bacterium is *Escherichia coli*.
16. The method of claim 12 wherein said bacterium is a member of the genus *Pseudomonas*.
17. The method of claim 16 wherein said bacterium is *Pseudomonas aeruginosa*.
18. The method of claim 8 wherein said host microorganism is a yeast.
19. The method of claim 8 wherein said yeast is *Saccharomyces cerevisiae*.
20. The method of claim 8 wherein said inhibitor is harvested prior to being caused to assume said active, tertiary structure.
21. The method of claim 8 wherein said inhibitor is caused to assume said active, tertiary structure prior to being harvested.
22. A metalloproteinase inhibitor which is biologically equivalent to the collagenase inhibitor isolable from human skin fibroblasts produced by the method of claim 8.
23. The microorganism C600/pUC9-F5/237P10 having ATCC Accession No. 53003.
24. The portable DNA sequence of claim 1 wherein said nucleotide sequence is:

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      10      20      30      40      50      60
GGCCATCGCC GCAGATCCAG CGCCCAGAGA GACACCAGAG AACCCACCAT GGGCCCCTTT

      70      80      90     100     110     120
GACCCCTGGC TTCTGCATCC TGTGTTGCT GTGGCTGATA GCCCAGCAG GGCCTGCACC

     130     140     150     160     170     180
TGTGTCCCAC CCCACCCACA GACGGCCTTC TGCAATTCCG ACCTCGTCAT CAGGGCCAAG

     190     200     210     220     230     240
TTCGTGGGGA CACCAGAAGT CAACCAGACC ACCTTATACC AGCGTTATGA GATCAAGATG
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250	260	270	280	290	300
ACCAAGATGT	ATAAAGGGTT	CCAAGCCTTA	GGGGATGCCG	CTGACATCCG	GTTCGTCTAC
310	320	330	340	350	360
ACCCCCGCCA	TGGAGAGTGT	CTGCGGATAC	TTCCACAGGT	CCCACAACCG	CAGCGAGGAG
370	380	390	400	410	420
TTTCTCATTG	CTGGAAAAGT	GCAGGATGGA	CTCTTGACAC	TCACTACCTG	CAGTTTCGTG
430	440	450	460	470	480
GCTCCCTGGA	ACAGCCTGAG	CTTAGCTCAG	CGCCGGGGCT	TCACCAAGAC	CTACACTGTT
490	500	510	520	530	540
GGCTGTGAGG	AATGCACAGT	GTTTCCCTGT	TTATCCATCC	CCTGCAAAGT	GCAGAGTGGC
550	560	570	580	590	600
ACTCATTGCT	TGTGGACGGA	CCAGCTCCTC	CAAGGCTCTG	AAAAGGGCTT	CCAGTCCCGT
610	620	630	640	650	660
CACCTTGCCCT	GCCTGCCTCG	GGAGCCAGGG	CTGTGCACCT	GGCAGTCCCT	GCGGTCCCAG
670	680	690	700	710	720
ATAGCCTGAA	TCCTGCCCCG	AGTGGAAGCT	GAAGCCTGCA	CAGTGTCCAC	CCTGTTCCCA
730	740	750	760	770	780
CTCCCATCTT	TCTTCCGGAC	AATGAAATAA	AGAGTTACCA	CCCAGCAAAA	AAAAAAAGGA